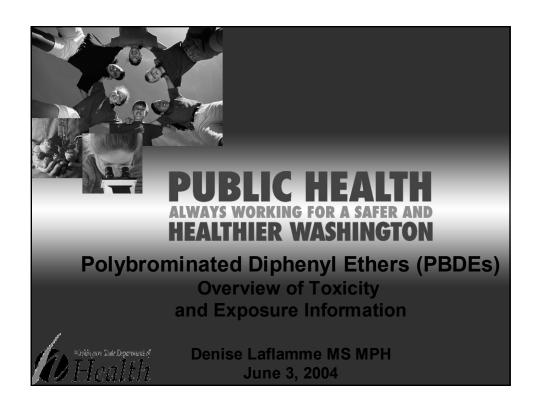
Polybrominated Diphenyl Ethers (PBDEs)

Overview of Toxicity and Exposure Information

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Toxicity Studies

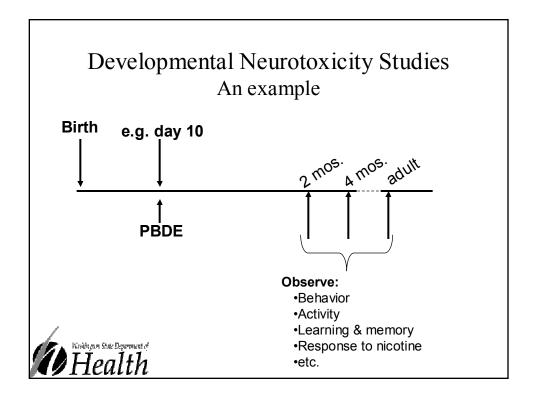
- In rats and mice
- Toxicity: penta > octa > deca
- Different effects seen for different congeners



Animal Toxicity Studies

- Development neurotoxicity
 - Perinatal/neonatal exposures
 - delays in sensory/motor development
 - Impaired learning and memory function
 - Effects on spontaneous motor activity (hyperactivity)
 - Permanent changes worsens with age
 - Additive effects with PCBs





Animal Toxicity Studies

- Thyroid Effects
 - Reduction in thyroid hormone levels in blood
 - Possible mechanisms:
 - PBDE metabolites interfere with binding to thyroid hormone transport protein
 - PBDE increases metabolism of thyroid hormone
 - The developing organism is especially sensitive to changes in thyroid function
 - Additive effects with PCBs



Toxicity Studies

- Reproductive effects
 - male and female
- Fetal toxicity
 - lower than maternally toxic doses
- Cancer
 - Deca (high doses)



Pharmacokinetics of PBDEs

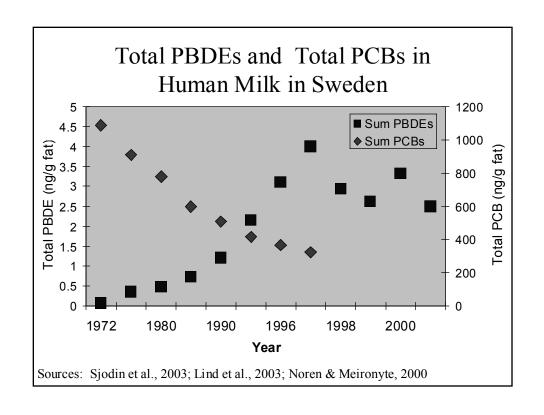
- Higher brominated PBDEs are poorly absorbed, e.g. deca
 - Deca can break down to lower brominated compounds
- Distribute in fat (lipid) depending on number of bromines
 - Why levels are adjusted for lipid
- Several metabolic products
- Mainly excreted in feces

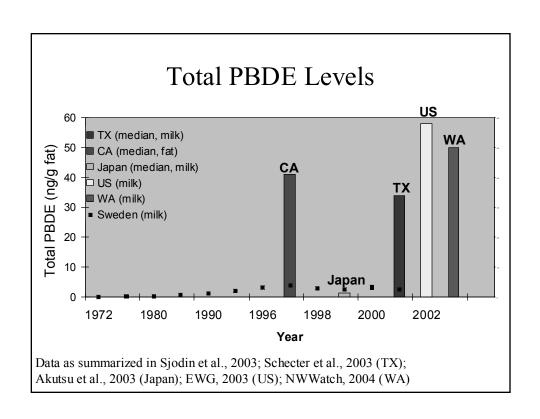


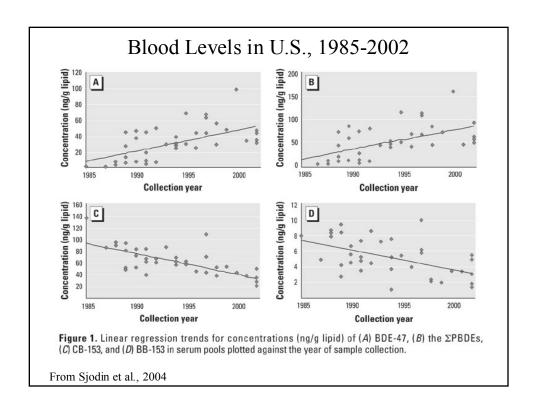
Human Studies

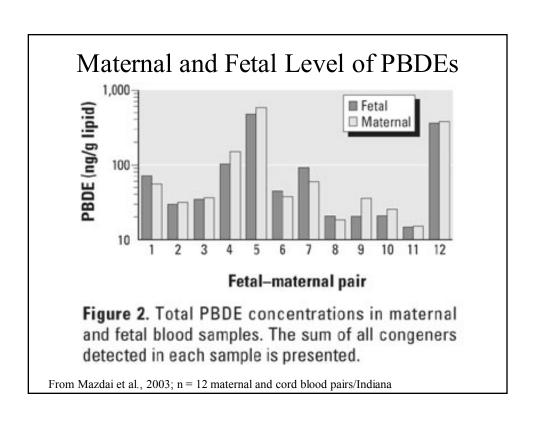
- Lack of epidemiological evidence
- Biomonitoring shows that people carry PBDEs in their bodies
 - General population
 - Some occupational groups

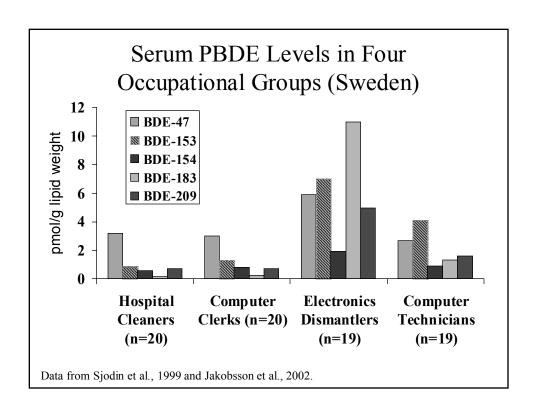












PBDEs in People

- PBDEs have been found in blood, fat and breastmilk
- U.S. levels of PBDEs in breast milk are 10-100 higher than in Europe or Japan
- U.S. levels of PBDE in blood are increasing
- Data from Sweden indicate exposures associated with some occupations
- Levels in cord blood (fetal) are similar to maternal levels



Margin of exposure appears low

- There is wide variability in reported PBDE levels in the U.S. It is estimated that 5% of women have >= 300 ng/g lipid
- Comparing this level to effects levels in rodent studies indicates that the margin of safety may be low for many individuals.

Reference: McDonald, 2004



Sources of PBDE Exposure

- PBDEs have been found in:
 - Foods
 - Dust (household and workplace)
 - Sewage sludge
 - Soil
 - Sediment
 - Biota (fish, marine mammals, birds)
 - Indoor and outdoor air



PBDEs in Food

- Food
 - PBDE tissue levels related to fish consumption (Sweden and Japan)
 - Studies of PBDE in food in countries outside U.S. (Spain, UK and Japan), indicate fish as large contributor to PBDE intake.
 - Contribution from food not well known for U.S.



PBDEs in Dust

- PBDEs associated with particles versus in gas phase
- Recent studies have found PBDEs in dust:
 - MA (2003) 89 homes
 - Europe (2001) Parliament buildings
 - US (2004) 10 homes
- Indoors (urban) > outdoors



In Summary

- Structure of PBDEs similar to PCBs and thyroxine, a thyroid hormone
- PBDEs associated with developmental neurotoxicity, changes in the thyroid system, reproductive effects and cancer in rodent studies
- PBDEs have been detected in human breast milk, blood and fat.
 - U.S. levels of PBDEs in human breast milk are 10-100 higher than levels in Europe.
 - U.S. blood levels are increasing.



In Summary

- Margin of safety appears to be low
- PBDEs are found in many media:
 - Including biota, foods, biosolids, dust, air
- Occupational exposures identified.
- It is unclear which PBDE sources contribute the most to existing human levels of PBDE in the U.S.



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